**IN THE UNITED STATES DISTRICT COURT FOR THE WESTERN DISTRICT OF MISSOURI CENTRAL DIVISION**

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| CHRISTINE WINTER, Individually, and as Personal Representative of the Estate of RUTH BALDWIN, | ) | |
| Plaintiff, | ) | |
| v. | ) | No. 06-4049-CV-C-MJW |
| NOVARTIS PHARMACEUTICALS CORPORATION, | ) | |
| Defendant. | ) | |

## ORDER

## I. Factual Background

Plaintiff Christine L. Winter, individually, and as Personal Representative of the Estate of Ruth Baldwin, deceased, claims that defendant Novartis Pharmaceuticals Corporation (NPC) caused Ms. Baldwin to develop osteonecrosis of the jaw (ONJ) by producing and marketing its drugs Aredia and Zometa.

Ms. Baldwin was a citizen and resident of the State of Missouri. NPC is a Delaware corporation, headquartered in the State of New Jersey, which produced and marketed the drugs Aredia and Zometa.

Aredia and Zometa have been frequently prescribed to patients with metatastic breast cancer since the Federal Drug Administration (FDA) approved Aredia in 1998. The FDA also approved NPC's labeling at that time. On September 26, 2003, NPC informed the FDA that it was changing its package insert to discuss the occurrence of ONJ in patients using bisphosphonates such as Zometa. In February 2004, at the request of the FDA, NPC again changed its package insert to discuss the risk factors of ONJ and to counsel against dental surgery "as recovery may be prolonged." (Doc. 109 at 19.) In August 2004, NPC revised this language again to discuss the risks of ONJ in more detail and to caution against dental surgery, stating, "For patients who develop ONJ [osteonecrosis of the jaw] while on bisphosphonate therapy,

dental surgery may exacerbate the condition." (Doc. 109 at 19.) The parties agree that NPC implemented these changes, but do not agree on when these changes actually reached physicians in the field. NPC highlighted these latest changes in a "Dear Doctor" letter dated September 24, 2004, but the parties dispute whether Dr. Hueser, Ms. Baldwin's oncologist, ever received this letter.

In July 2003, Ms. Baldwin was diagnosed with recurrent breast cancer with metastases to her spine and liver. On July 24, 2003, Ms. Baldwin's oncologist, Dr. James Hueser, prescribed Aredia to Ms. Baldwin. In September 2003, Dr. Hueser changed Ms. Baldwin's prescription from Aredia to Zometa. Ms. Baldwin received her last treatment of Zometa in October 2004. On November 11, 2004, Dr. Hueser decided to stop Ms. Baldwin's Zometa treatment because she had developed ONJ, which he believed to be an effect of Zometa. Dr. Hueser cannot recall a patient with metastases to whom he did not prescribe Aredia or Zometa prior to that point. Dr. Hueser has testified he never read the package inserts for Aredia and Zometa while practicing as an oncologist, but that this was because Novartis produced them in a way that made them useless to a practitioner.

Dr. Douglas Miller was Ms. Baldwin's dentist from January 1998 to September 2006. On November 6, 2003, Dr. Miller extracted Ms. Baldwin's tooth # 31, and on September 9, 2004, Dr. Miller extracted Ms. Baldwin's tooth # 30. On October 25, 2004, Dr. Miller referred Ms. Baldwin to an oral surgeon, Dr. Timothy Coyle, due to her complaints of discomfort in the area of her mouth from which Dr. Miller had extracted tooth # 30. On October 26, 2004, Dr. Coyle informed Dr. Miller that Ms. Baldwin had developed ONJ from her bisphosphonate chemotherapy, precipitated by tooth extractions.

Dr. Miller has testified that had he known about the relationship between bisphosphonates and ONJ, he would have considered alternatives to tooth extraction on Ms. Baldwin. Dr. Miller has never prescribed Aredia or Zometa. Dr. Miller's treatment notes do not reflect that Ms. Baldwin ever informed him she was being treated for cancer at any point before she was diagnosed with ONJ.

NPC has filed motions in limine to exclude the testimony of three of plaintiff's expert witnesses.

## II. Legal Standard

The admission of expert testimony is governed by Rule 702 of the Federal Rules of Evidence. In Daubert v. Merrill-Dow Pharm., Inc., 509 U.S. 579 (1993), the Supreme Court stated that "a rigid 'general acceptance' requirement would be at odds with the 'liberal thrust' of the Federal Rules and their 'general approach of relaxing the traditional barriers to 'opinion testimony.'" 509 U.S. 588 (quoting Beech Aircraft Corp. v. Rainey, 488 U.S. 153, 169 (1988) (citing Fed. R. Evid. 701-05)). Daubert was not written as a barrier to the admission of expert testimony, but as the rejection of a rigid prerequisite to admissibility incompatible with Rule 702. Essentially, to be admissible under Rule 702, the proffered testimony need only be relevant and reliable. Daubert, 509 U.S. at 589. Further, "evidentiary reliability" means only that the evidence is trustworthy because "it would be unreasonable to conclude that the subject of scientific testimony must be 'known' to a certainty. . . ." Daubert at 590. The Eighth Circuit has stated that the proponent of the expert testimony must show by a preponderance of the evidence that the expert is qualified to give the opinion and that his or her methodology is scientifically valid. Marmo v. Tyson Fresh Meats, Inc., 457 F.3d 748, 757-58. (8th Cir. 2006).

Moreover, in Kumho Tire Co. v. Carmichael, 526 U.S. 137 (1999), the Court reiterated that the factors identified in Daubert may or may not be pertinent in assessing reliability. The conclusion, in our view, is that we can neither rule out, nor rule in, for all cases and for all time the applicability of the factors mentioned in Daubert, nor can we now do so for subsets of cases categorized by category of expert or by kind of evidence. Too much depends upon the particular circumstances of the particular case at issue. Daubert made clear that its list of factors was not meant to be definitive. 526 U.S. at 150-51.

The Eighth Circuit has recognized that the factual basis of an expert opinion goes to the credibility or weight of the testimony rather than its admissibility – it is up to the opposing party to explore the reasons for that opinion in cross-examination. Larson v. Kempker, 414 F.3d 936, 941 (8th Cir. 2005) (internal citations omitted). Only when an expert opinion is so "fundamentally unsupported that it can offer no assistance to the jury" should the testimony be excluded. Id. (citing Loudermill v. Dow Chemical Co., 863 F.2d 566, 570 (8th Cir. 1988)).

## III. Motion in Limine to Exclude Testimony of Dr. Suzanne Parisian

On May 2, 2011, defendant Novartis Pharmaceuticals Corporation (NPC) filed a motion in limine to exclude the expert testimony of plaintiff's expert, Dr. Suzanne Parisian. (Doc. 41.) Plaintiff Christine Winter filed suggestions in opposition, and defendant filed reply suggestions in support. In addition, on February 29, 2012, the court heard argument from counsel for plaintiff and defendant.

Dr. Suzanne Parisian received her medical degree from the University of South Florida and is board certified in Anatomic and Clinical Pathology. She also has a masters in biology from the University of Central Florida. During her career, she has worked in a number of fields related to the health care industry. From 1991 to 1995, she worked with the United States Public Health Care Service, where she was assigned to the Center for Devices and Radiological Health at the FDA. Concurrently, Dr. Parisian was a medical officer with the FDA in the Office of Health Affairs where she prepared health hazard and health risk assessments, and reviewed adverse event reports, product labeling, and other pertinent medical literature. In this position, she also presided over one hundred health care risk assessments and advised the FDA on the health risk issues for the public. She further worked with the Office of Device Evaluation, where she reviewed proposed clinical trials and trained other FDA medical officers to evaluate medical labeling. Since her departure from the FDA in 1995, Dr. Parisian has spent a great deal of time testifying as an expert witness on the FDA and its regulations. See Deutsch v. Novartis Pharm. Corp., Nos. 09-CV-4677, 09-CV-4678, 2011 WL 790702, at *43 (listing cases) (E.D.N.Y. March 8, 2011.)

NPC's motion to exclude Dr. Parisian's testimony argues her testimony should be precluded as follows:

1. Dr. Parisian's testimony should be excluded in its entirety because it is largely irrelevant, and she is not qualified to offer any of her potentially relevant opinions;

2. If not excluded in its entirety, the Court should exclude specific portions of her testimony that are irrelevant, speculative, unhelpful to the jury, or otherwise exceed the scope of proper expert testimony as follows:

(a) the Court should preclude Dr. Parisian from simply quoting or summarizing documents, arguing plaintiff's case and offering legal conclusions;

(b) the Court should exclude Dr. Parisian's opinions about NPC's intent and unspecified industry standards because they are speculative and exceed the scope of expert testimony;

(c) the Court should exclude Dr. Parisian's opinions that do not "fit" the relevant inquiry in this case;

(d) the Court should exclude Dr. Parisian's testimony about labeling because it is unhelpful to the jury and beyond the scope of her expertise;

(e) the Court should exclude Dr. Parisian's testimony about ghost writing and undisclosed company funding of publications for lack of foundation;

and

3. Dr. Parisian is unqualified to offer an opinion on causation or the diagnosis of ONJ. (Doc. 42 at 2.).

Plaintiff disagrees and argues that Dr. Parisian's testimony should be admitted in its entirety. NPC has requested a Daubert hearing which plaintiff opposes because of the extensive briefing and numerous court opinions that are already available for review from throughout the country concerning Dr. Parisian's testimony and qualifications. The Court agrees with plaintiff. There is an extensive amount of material available to the Court concerning Dr. Parisian and the Court does not believe a Daubert hearing at this late stage would be helpful or is necessary in order to rule. The Court has reviewed a large volume of material concerning Dr. Parisian, and hearing further testimony is unnecessary. A trial court is not required to hold a Daubert hearing so long as it assesses the relevance and reliability of the expert's testimony. See United States v. Smithers, 212 F.3d 306, 324 (6th Cir. 2000); Greenwell v. Boatwright, 184 F.3d 492, 498 (6th Cir. 1999); Krueger v. Johnson and Johnson Professional, Inc., 160 F. Supp. 2d 1026 (S.D. Iowa, 2001).

Conclusions regarding Dr. Parisian

*A. Dr. Parisian is qualified to testify as an expert.*

Dr. Parisian's testimony as an expert has been repeatedly allowed in both state and federal courts throughout the United States in the bisphosphonate ONJ litigation. Dr. Parisian's curriculum vitae clearly reveals she is a qualified expert witness in this area. (Doc. 67, PX 11.)

Dr. Parisian has been proffered as a regulatory expert to opine on regulatory and labeling issues and is qualified to testify on these issues under Rule 702, which, consistent with Daubert, sets forth the standard for admissibility. A person is qualified to testify as an expert under Rule 702 "by knowledge, skill, experience, or training." Dr. Parisian is clearly qualified as an expert and her testimony is relevant to the issues in this case. However, certain limited parts of her testimony will be excluded. Virtually all of the courts (except Hogan v. Novartis, No. 06-CV-00260 (E.D.N.Y. April 15. 2011)) in the bisphosphonate ONJ litigation have found that her testimony satisfies the requirements of Rule 702 and Daubert. Here, the Court believes her testimony will help the lay jury understand the issue of the adequacy of warning and labeling, which "must be viewed, in part, in the context of the FDA's role in the approval and marketing of pharmaceuticals. Dr. Parisian's testimony on the role of the FDA and the pharmaceutical industry in general and regarding new drug approvals is relevant to establish a context in which to analyze the reasonableness of NPC's actions regarding Zometa." Stevens v. Novartis, (Order of Judge Larson at p.3, Ex. 1).

"The touchstone for the admissibility of expert testimony is whether it will assist or be helpful to the trier of fact." Lee v. Andersen, 616 F.3d 803 (8th Cir. 2010), cert. denied, 131 S. Ct. ___ (2010). Dr. Parisian's testimony is reliable and will assist the jury.

In opposition to the large number of cases holding that Dr. Parisian is an expert and allowing her to testify, including in every bisphosphonate case ever tried against a drug company, except Hogan where the court ruled pretrial that the word "FDA" was to be excluded from the case, NPC relies on In Re Trasylol Prods. Liab. Litig., 709 F. Supp. 2d 1323 (S.D. Fla. 2010). The Trasylol court involved a different report about a different drug before it, involving different plaintiffs' counsel. Except for these minor exceptions, almost all courts have previously admitted the majority of Dr. Parisian's testimony.

*B. Specific areas of Dr. Parisian's testimony.*

Regarding the remaining areas of Dr. Parisian's testimony to which NPC has objected, the Court rules as follows:

1. NPC's motion to exclude Dr. Parisian's testimony in its entirety at trial (Doc. 41) is denied.

2. NPC's motion to exclude specific portions of Dr. Parisian's testimony is granted, in part, and denied, in part.

(a) The Court denies NPC's motion to preclude Dr. Parisian from quoting or summarizing documents. Dr. Parisian may testify about industry standards for the pharmaceutical industry and whether, based upon her expertise and review of NPC documents, NPC may have violated industry standards.

(b) The Court grants NPC's motion to exclude Dr. Parisian's opinions about NPC's intent and personal opinions about NPC's and its employees' states of mind, motivations, or subjective intent.

(c) The Court denies, in part, NPC's motion to exclude discussion by Dr. Parisian of clinical trials and other bisphosphonate drugs regulated by the FDA. Dr. Parisian may testify concerning these areas if she demonstrates the testimony is relevant to the issues in this case. The Court may reconsider its ruling in this area if Dr. Parisian's testimony strays too far from the issues the jury here must decide and a timely objection is made at trial.

(d) The Court denies NPC's motion to exclude Dr. Parisian's testimony about labeling and warnings. She may testify on the issue of what the regulatory requirements are for regulatory analysis of causation for purposes of labeling.

(e) NPC's motion to exclude Dr. Parisian's testimony about ghostwriting and undisclosed company funding of publications is denied as moot. Plaintiff confirmed at the pretrial conference held on February 29, 2012, that she will not offer evidence on these issues during the trial.

3. The Court grants NPC's motion to exclude Dr. Parisian's testimony and opinion as to whether bisphosphonates caused ONJ in this case.

## IV. Motion in Limine to Exclude Testimony of Dr. Robert Marx

On May 2, 2011, defendant filed a motion in limine to exclude the expert testimony of plaintiff's expert, Dr. Robert Marx, D.D.S. (Doc. 32.) Plaintiff filed suggestions in opposition, and defendant filed reply suggestions in support.

Dr. Marx is a board-certified oral and maxillofacial surgeon and has worked for the University of Miami School of Medicine as a Professor of Surgery since 1984. He is currently the Chief of the Division of Oral and Maxillofacial Surgery for the University. Dr. Marx's work at the Medical School includes removal of benign and malignant tumors, reconstructive surgery, and treatment and removal of diseased or dead jawbone cause by irradiation (osteoradionecrosis), osteomyelitis, osteopetrosis, and ONJ. Dr. Marx is a well-published surgeon, who is well

recognized for his many accomplishments in his field of expertise. He has been in the forefront of studying the connection between ONJ and bisphosphonate drugs.

NPC's motion to exclude Dr. Marx's testimony argues that his testimony should be precluded on the following issues:

1. His testimony as to general causation based on adverse event reports;

2. His testimony as to what he believes the biological mechanism is by which biphosphonate drugs cause ONJ;

3. Dental treatment measures he believes will help prevent BIONJ;

4. His opinion that certain patients in NPC's clinical trials had BIONJ;

5. His opinion that the design of the clinical trials was deficient; and

6. His opinion that NPC acted in "bad faith" when they attempted to manipulate an article for publication in the Journal of Clinical Oncology.

Plaintiff argues that the Court should outright deny the motion to exclude testimony of Dr. Marx. Plaintiff argues that NPC's motion ignores the prior rulings of the Multi-District Litigation (MDL) court and that Dr. Marx's proffered testimony meets the standard required for expert testimony. Plaintiff argues that the objections made by NPC are issues for cross-examination of Dr. Marx, not exclusion of his testimony.

*A. General causation*.

NPC argues that Dr. Marx's causation testimony, which is based, in part, on event reports submitted to the FDA and NPC is fundamentally flawed. NPC argues that the event reports merely present anecdotes that do not rise to the level of scientifically reliable causation proof.

Plaintiff argues that this argument has already been made and rejected in the MDL case. Plaintiff argues that the MDL case has already provided that Dr. Marx may provide general causation opinions based on adverse event reports, including those he has seen as reported cases.

Upon review, this Court finds that the MDL court has already denied NPC's motion seeking to exclude Dr. Marx's litigation-wide testimony as to causation. Dr. Marx's testimony was found to be sufficient under Daubert as to the general and specific causal connection between Aredia and Zometa and ONJ. Since this objection has been ruled, it need not be revisited. However, the Court notes that a review of the records leads to the same conclusion.

Clearly, Dr. Marx's testimony as to causation is based on his scientific knowledge and expertise as to these specific drugs and their connection to ONJ. Dr. Marx's offered testimony is based on scientifically valid principles. NPC can cross-examine Dr. Marx on the bases for his causation expert opinion, including any reliance on adverse event reports. NPC's motion to exclude this causation testimony of Dr. Marx is denied.

*B. The biological mechanism by which bisphosphonate drugs cause ONJ.*

NPC argues there is a scientific dispute as to the biological mechanism by which bisphosphonate drugs allegedly cause ONJ. Defendant further argues that Dr. Marx has no scientifically reliable support for his opinions on biological mechanism.

Plaintiff argues that this issue was also addressed by the MDL court, and that a challenge by NPC regarding scientific dispute is improperly filed under Daubert. Plaintiff argues that Dr. Marx has conducted research, published peer-reviewed articles, and essentially acted as an authority on the relationship between bisphosphonates and ONJ, and his academic involvement and background in identifying and studying patients with ONJ qualifies him to give his opinion on the subject.

Upon review, this Court again finds that this issue appears to have already been resolved in plaintiff's favor at the MDL level, and thus, it need not be revisited. The Court notes, however, that the documents in this case are sufficient to establish the necessary basis, under Daubert, for Dr. Marx's testimony on this issue. Dr. Marx has extensive experience with ONJ and bisphosphonate drugs, and has conducted research in this area which has been published and subjected to peer review. Again, NPC can address their arguments regarding Dr. Marx's expertise in this area upon cross-examination. NPC's motion to exclude this testimony is denied.

*C. Dental treatment measures that Dr. Marx believes help prevent BIONJ.*

NPC argues that Dr. Marx has no scientifically reliable basis on which to opine that dental treatment measures actually prevent bisphosphonate patients from developing ONJ. NPC argues that this testimony is speculation by Dr. Marx, and is not admissible as expert testimony.

Plaintiff argues again that this issue was also resolved with the MDL court, and that the court denied NPC's motion to exclude such testimony under Daubert. Plaintiff further argues

that NPC's challenge to the reliability of noncontrolled studies go to the weight, not the admissibility, of Dr. Marx's opinion.

Upon review, the MDL court did deny NPC's Daubert motion on this issue. Moreover, the expert report of Dr. Marx clearly shows his expertise in BIONJ and treatment. Accordingly, Dr. Marx's testimony regarding dental treatment, either before or after the development of BIONJ, is within his realm of expertise. Under Daubert, absolute certainty or general acceptance as to new theories is not a prerequisite to admissibility of expert testimony when the testimony is based on reliable methodology. Daubert at 588. To the extent there is conflicting evidence regarding the effectiveness of dental treatment measures in preventing BIONJ, defendant can cross-examine the witness on this issue. NPC's motion to exclude this testimony is denied

*D. Dr. Marx's opinion that certain patients in NPC's clinical trials had BIONJ.*

NPC argues that Dr. Marx's post-hoc diagnosis determining that five of the six patients in the NPC clinical trials in fact had BIONJ is contrary to his own methodology for determining whether patients have BIONJ. Specifically, NPC argues that, contrary to Dr. Marx's methodology for diagnosis, including exposed bone for eight weeks, he diagnosed these patients without documentation of exposed bone.

Plaintiff argues that the records at issue were created in 1999 or 2000, a time which predates the existence of the definition of bisphosphonate-related, associated, or induced ONJ. Plaintiff argues that because exposed bone was not yet known to be a relevant indicator of BIONJ, the records would not necessarily reflect the presence or absence of exposed bone. Therefore, Dr. Marx can reasonably consider not only whether the bone was noted on the chart, but other circumstantial evidence of BIONJ.

Upon review, this Court again notes the allowance of this testimony by the MDL court as sufficient under Daubert. The records were created at a time which predated the definition of bisphosphonate-related, associated or induced osteonecrosis. With this limitation, it is reasonable for Dr. Marx to consider not only whether exposed bone was noted on the chart, but also to look at the circumstantial evidence of BIONJ. Again, cross-examination of Dr. Marx remains available to NPC for purposes of showing the strength of Dr. Marx's conclusions. Plaintiff's motion to exclude this testimony is denied.

*E. Dr. Marx's opinion that the design of the clinical trials was deficient.*

NPC argues that Dr. Marx lacks the experience required to address the issue, and his criticism is based on 20/20 hindsight rather than reliable methodology. NPC argues that Dr. Marx has admitted he has never planned or managed any clinical trials relating to any bisphosphonates or any clinical trials intended to study the effects of any other drugs on humans. NPC further points out that Dr. Marx has conceded he does not hold himself out as an expert in FDA regulations of drug companies and that he has never been involved in putting together a New Drug Application for submission to the FDA.

Plaintiff argues Dr. Marx need not have experience conducting clinical trials to criticize NPC's patently obvious failure to properly include any oral cavity specialist in its clinical trials. Alternatively, plaintiff argues that even if Dr. Marx's opinion criticizing NPC's clinical trials is excluded, he should not be precluded from commenting on the fact that certain information was not included in the clinical trials, or that certain examinations or surgeries were not performed during the clinical trial.

The Court notes that this issue was specifically not ruled on by the MDL court. Dr. Marx does not hold the necessary expertise to criticize the overall adequacy of NPC's clinical trials. There is no scientific basis on which Dr. Marx can give his expert opinion on this issue. However, Dr. Marx's testimony regarding the lack of records will be allowed to the extent necessary for Dr. Marx to explain his opinion on whether the clinical trials included patients with BIONJ. NPC's motion on this issue is, therefore, granted, in part, as set forth above.

*F. Dr. Marx's opinion that NPC acted in "bad faith" when they attempted to manipulate an article for publication in the Journal of Clinical Oncology.*

NPC argues that Dr. Marx's testimony runs afoul when it accuses NPC of trying to "manipulate" an article about ONJ, which he felt demonstrated "bad faith." NPC argues that Dr. Marx concedes this is his own personal opinion, and he cannot opine about NPC's state of mind.

Plaintiff argues Dr. Marx is competent to testify regarding the history of NPC's efforts to control the conclusions of the advisory boards it convened and pressures exerted upon himself and others to comport to NPC's wishes. Plaintiff argues that even if Dr. Marx is not permitted to testify as to his opinion that the actions of NPC were done in bad faith, Dr. Marx should not be

precluded from offering his expert opinion as to what information was available based on the relevant medical literature and Novartis internal comments. Plaintiff argues Dr. Marx should not be precluded from testifying as a fact witness about his experiences working with Novartis and Novartis employees.

This issue was also specifically not ruled by the MDL court. This Court finds that Dr. Marx's opinion that NPC's actions were done in bad faith has no proper basis of expertise. Dr. Marx cannot testify about the state of mind, intent or motives of NPC. However, Dr. Marx can testify as a fact witness. Contrary to the reply argument made by NPC, this Court believes the jury has sufficient ability to understand and not confuse Dr. Marx's testimony as an expert witness and his testimony as a fact witness regarding his own experiences in working with Novartis and its employees. Therefore, NPC's motion to exclude this testimony is granted, in part, as set forth above.

Conclusion Regarding Dr. Marx

1. NPC's motion to exclude the testimony of Dr. Marx in its entirety at trial is denied.

2. NPC's motion to exclude specific portions of Dr. Marx's testimony is granted, in part, and denied, in part, as follows:

(a) The Court denies NPC's motion to exclude the causation testimony of Dr. Marx.

(b) The Court denies NPC's motion to exclude the testimony of Dr. Marx regarding the biological mechanism by which bisphosphonate drugs cause ONJ.

(c) The Court denies NPC's motion to preclude the testimony of Dr. Marx regarding dental treatment measures that he believes help prevent BIONJ.

(d) The Court denies NPC's motion to exclude Dr. Marx's testimony regarding his opinion that certain patients in NPC's clinical trials had BIONJ.

(e) The Court grants, in part, NPC's motion to exclude Dr. Marx's opinion that the design of the clinical trials was deficient. However, Dr. Marx's testimony regarding the lack of records will be allowed to the extent necessary for him to explain his opinion on whether the clinical trials included patients with BIONJ. NPC's motion on this issue is granted in all other respects.

(f) The Court grants, in part, NPC's motion to exclude Dr. Marx's testimony regarding his opinion that NPC acted in "bad faith" when it attempted to manipulate an article for publication in the Journal of Clinical Oncology. However, Dr. Marx can testify as a fact witness regarding his own experiences working with NPC and NPC employees. NPC's motion on this issue is granted in all other respects.

**V. Motion in Limine to Exclude Testimony of Professor Wayne Ray, Ph.D.**

Defendant filed a motion in limine to exclude the testimony of plaintiff's expert, Wayne Ray, Ph.D. (Doc. 36.) Plaintiff has filed suggestions in opposition and NPC has filed a reply in support.

Dr. Ray is Professor of Preventative Medicine, Director of the Division of Pharmacoepidemiology and Director of the Master of Public Health Program at Vanderbilt University School of Medicine. Dr. Ray is an epidemiologist and has been involved in pharmacoepidemiologic research for more than thirty years. He has served and continues to serve as a principle investigator for many studies and research, including multiple FDA contracts for research, as well as contracts for research for the National Institute of Health and Centers for Disease Control. Dr. Ray evaluates and designs studies that determine whether or not there is evidence that a medication causes an adverse reaction. As a principle investigator, Dr. Ray provides advice and performs studies on adverse medication reactions, and assessment of the appropriateness of medication use. Dr. Ray has served as a member on two occasions for FDA Advisory Committees providing expertise in study design and methodology. Dr. Ray has also served as a member of several National Institutes of Health and Centers for Disease Control study section panels in which he was required to evaluate the methodology of studies submitted for potential federal research funding.

Plaintiff hired Wayne Ray, Ph.D., to offer his expert opinion as to (1) whether there is a strong association between the use of IV bisphosphonates in cancer patients and subsequent ONJ; and (2) to establish to a reasonable degree of medical certainty whether bisphosphonates cause ONJ in cancer patients.

NPC's Challenges Seeking to Preclude Testimony of Dr. Ray

*A. Dr. Ray's Qualifications and Methodology.*

NPC challenges Dr. Ray's qualifications and methodology for providing opinions in this case, including challenges to qualification to perform meta-analysis. Plaintiff asserts Dr. Ray is extremely well qualified in his field of expertise and clearly qualified to conduct this study utilizing meta-analysis. Plaintiff argues this is not some new type of study that Dr. Ray has come up with for this litigation, as alleged by NPC; rather, it is a type of study that Dr. Ray has substantial experience in utilizing.

It is clear the methods followed and analyses performed by Dr. Ray in reaching his opinions set forth in his expert report are consistent with the methodologies used by others in Dr. Ray's field of expertise. Dr. Ray has decades of experience in the field of pharmacoepidimiologic research where he has designed, executed, analyzed and evaluated studies on the adverse effects of medication, as is the issue in this case. Large numbers of companies and organizations, including governmental organizations such as the FDA, have utilized Dr. Ray and his studies, thus, affirming their value. Clearly, Dr. Ray has the expertise to perform the study in this case, including the meta-analysis, and to give his opinions. NPC's motion to preclude Dr. Ray's testimony on these bases is denied.

*B. Specific challenge to Dr. Ray's opinion on relative risk and attributable risk in Table 5 meta-analysis.*

NPC argues that Dr. Ray's findings on relative risk and attributable risk in Table 5 used faulty methodology. NPC argues Dr. Ray does not have the expertise to compile and present the Table 5 meta-analysis, and challenges the methodology of the analysis, including 1) Dr. Ray's decision to use the three-month cut-point as unreliable methodology; 2) Dr. Ray's use of patients as their own controls; and 3) allegations that Dr. Ray failed to account for potential distorting impact of confounders.

Plaintiff argues that certainly Dr. Ray's expertise and experience qualify him to compile and present the Table 5 meta-analysis and that his methodology is consistent with the methodologies used by others in his field. Plaintiff argues that Dr. Ray's use of the three-month

cut-point and patients as their own controls were thoroughly explained by Dr. Ray in his study. Additionally, plaintiff argues that Dr. Ray's study did, in fact, account for potential confounders.

As set forth above, Dr. Ray has the expertise and is qualified to compile and present the Table 5 meta-analysis and opine as to relative risk and attributable risk. As to methodology, a review of Dr. Ray's report shows a detailed explanation for creation of a control group consisting of patients who received less than three months of IV BP therapy, as well as for using each patient as their own control. NPC's challenges to this methodology go to the weight of the study, rather than its admissibility. NPC can make its challenges on cross-examination.

NPC's argument that Dr. Ray failed to make a statistical adjustment to account for potential confounders, again goes to weight. The Court further notes that Dr. Ray gave extensive discussion in his report to alternative explanations.

NPC's motion to exclude this testimony is denied.

*C. NPC seeks to exclude Dr. Ray's "Bradford-Hills Analysis" as unreliable.*

In response to NPC's challenge to Dr. Ray's use of the Bradford-Hills analysis, plaintiff argues that the Bradford-Hill analysis is an acceptable methodology for assessing causation.

Dr. Ray is extremely well qualified in his field of expertise on which he has submitted his expert report, and states that in his field, he has used this Bradford-Hills analysis frequently. Dr. Ray's report shows his familiarity with the methodology. The report discusses all nine of the criterion used to determine a causal relationship under this analysis. NPC's arguments go to the weight, rather than the admissibility of Dr. Ray's opinions based on the Bradford-Hill analysis. NPC's motion on this issue is denied.

*D. NPC seeks to exclude Dr. Ray's Table 6 Meta-analysis as unreliable.*

NPC argues that Dr. Ray is unqualified to perform and did not employ reliable methodology in performing his Table 6 meta-analysis.

Plaintiff argues Dr. Ray is qualified, and moreover, that his methodology properly considered duration of therapy. Plaintiff argues that because zoledronic acid had been on the market a shorter time than pamidronate, patients receiving zoledronic acid are likely to have a shorter duration of therapy than those on pamidronate. Plaintiff argues this fact sufficiently accounted for the duration of therapy.

Although the Court believes Dr. Ray is well qualified to conduct this analysis, the failure to accurately account for duration of therapy when comparing risk between zoledronic acid and pamidronate makes Table 6 unreliable. Compared with Dr. Ray's Table 5 analysis, Table 6 fails to specifically account for the passage of time over which patients received zoledronic acid versus receiving pamidronate. Although Dr. Ray states there need be no control for the passage of time because zoledronic acid was on the market for a shorter period of time than pamidronate and thus patients receiving this drug were likely to have shorter duration in therapy, this explanation is not supported by any scholarly articles or otherwise, and is inconsistent with Dr. Ray's own methodology which clearly asserts that passage of time, or duration that a patient is on bisphosphonates is associated with increased risk of ONJ. NPC's motion to exclude this portion of Dr. Ray's Table 6 meta-analysis report and corresponding testimony is granted.

*E. NPC moves to preclude Dr. Ray from opining as to causation based on case and adverse event ("AE") reports.*

NPC argues that Dr. Ray should be precluded from giving causation testimony based on scientifically unreliable information in case reports and AE reports.

Plaintiff argues that NPC's motion to exclude Dr. Ray's testimony based on Dr. Ray's failure to dissect the case and AE reports for potential flaws, clearly goes to the weight of Dr. Ray's conclusions, not to its admissibility.

The Court notes that NPC's argument as to reliance on the case and AE reports was also raised in the MDL court as to Dr. Marx and others, and that these objections were rejected by the MDL court, and have also been rejected by this Court. This Court again affirms that these reports can be used and relied upon. Dr. Ray may rely on the existence of the case reports and the AE reports, even those he has not personally reviewed. NPC's motion to exclude this testimony of Dr. Ray is denied.

*F. NPC moves to preclude Dr. Ray from opining that roughly 5% of IV BP patients develop ONJ and that ONJ is "not rare" in IV BP patients.*

NPC argues that Dr. Ray's opinion that five percent of IV BP patients develop ONJ is based on unreliable case and AE reports, and therefore, should be excluded. NPC also argues that Dr. Ray should not be able to opine that ONJ is not rare in IV patients because this statement is Ray's personal opinion, and does not amount to reliable methodology.

Plaintiff argues that the case and AE reports can be properly relied upon in reaching Dr. Ray's opinions. Plaintiff further argues that Dr. Ray may give his opinion of "not rare" because it is properly based on his review of the studies of patients treated with IV bisphosphonates.

As set forth above, Dr. Ray's opinions relying on the case and AE reports are admissible, and therefore, Dr. Ray can opine that roughly five percent of IV BP patients develop ONJ. However, NPC's motion to exclude the testimony of Dr. Ray as to his specific statement that he believes ONJ is not rare in BP patients is granted. This opinion is not the result of Dr. Ray applying the principles of his expertise to the facts in this case; rather, it is Dr. Ray's personal opinion as to the number of bisphosphonate IV patients shown to have ONJ in the reports he reviewed. Statements not made based on expertise, but merely an expert's subjective personal interpretation, are not admissible. Further, the Court notes that Dr. Ray confirms in his deposition that "not rare" does not have a specific number attached to its definition and is subjective. Dr. Ray's statement that ONJ is not rare in bisphosphonates patients is likely to lead a jury to believe this is a scientific representation.

*G. NPC seeks to exclude Dr. Ray's opinions regarding a clinical trial known as AZURE, and his opinions as to whether NPC should have done more to generate post-marketing data.*

NPC argues that Dr. Ray did not disclose this information in his expert report, and therefore, Dr. Ray should not be allowed to testify on these issues.

Plaintiff argues that NPC extensively cross-examined Dr. Ray on his opinions regarding the AZURE trial and post-marketing data during deposition and at another hearing within the MDL litigation. Plaintiff, therefore, argues that NPC cannot claim unfair surprise.

The Court agrees that Dr. Ray's comments on the AZURE clinical trial and post-marketing data do not amount to unfair surprise. Deposition testimony indicates Dr. Ray has been questioned extensively on his opinion on these issues by NPC attorneys. NPC does not argue that Dr. Ray's opinions are scientifically unreliable or that Dr. Ray lacks sufficient qualifications to opine on these issues. NPC's motion to exclude this testimony is denied.

*H. NPC moves to preclude Dr. Ray from testifying it is biologically plausible that IV BP drugs increase ONJ.*

NPC argues that Dr. Ray lacks the expertise and has no reliable methodology to give his biological plausibility opinions.

Plaintiff argues biological plausibility is one of the factors epidemiologists use to assess causation under the Bradford-Hill criterion, and therefore, Dr. Ray should be allowed to testify on this issue.

This Court agrees that Dr. Ray's testimony as to biological plausibility is directly linked to the Bradford-Hill criterion, and therefore, is admissible. As set forth above, Dr. Ray's expertise and background make him more than capable of performing the Bradford-Hill analysis. NPC's motion to exclude this testimony is denied.

*I. NPC moves to preclude Dr. Ray from testifying causation regarding ONJ could have been reached in 2003 at the time Dr. Marx's reports became available.*

NPC argues Dr. Ray cannot give this opinion because all of the papers Dr. Ray relied on in conducting his meta-analysis were published after 2003, and because causation has not been definitively established.

Plaintiff asserts there is no basis for excluding Dr. Ray's opinion on this issue.

The Court finds that Dr. Ray can provide this opinion. This opinion is not based on his review of the cohort studies from his meta-analysis, but on the initial report of Dr. Marx that reported 36 cases of BIONJ in September 2003, and on the increase in case reports and adverse event reports on which Dr. Ray finds there is no credible alternative explanation. Moreover, the fact that causation has not been definitely established does not prevent experts from opining on the likelihood of causation. Therefore, having found that Dr. Ray's opinion as to causation based on case reports and AE reports to be admissible, and the liberal standard of admissibility, NPC's motion to exclude this testimony is denied. Cross-examination is the proper avenue for NPC to challenge this opinion of Dr. Ray.

Conclusion Regarding Dr. Ray

1. NPC's motion to preclude the testimony of Dr. Ray is denied.

2. NPC's motion to in exclude specific portions of Dr. Ray's testimony is granted, in part ,and denied, in part, as follows:

(a) The Court denies NPC's challenge to Dr. Ray's qualifications and methodology.

(b) The Court denies NPC's specific challenge to Dr. Ray's testimony regarding his opinion on relative risk and attributable risk in Table 5 meta-analysis.

(c) The Court denies NPC's motion to exclude Dr. Ray's "Bradford-Hills Analysis" as unreliable.

(d) The Court grants NPC's motion to exclude Dr. Ray's Table 6 Meta-analysis as unreliable.

(e) The Court denies NPC's motion to preclude Dr. Ray from opining as to causation based on case and adverse event reports.

(f) The Court grants, in part, NPC's motion to preclude Dr. Ray from opining that roughly five percent of IV BP patients develop ONJ and that ONJ is "not rare" in IV BP patients. Dr. Ray may testify as to the number of IV BP patients shown to have ONJ in the reports he reviewed. He may not testify as to his specific statement that he believes ONJ is "not rare" in IV BP patients.

(g) The Court denies NPC's motion to exclude Dr. Ray's opinions regarding a clinical trial known as AZURE and his opinions as to whether NPC should have done more to generate post-marketing data.

(h) The Court denies NPC's motion to preclude Dr. Ray from testifying it is biologically plausible that IV BP drugs increase ONJ.

(i) The Court denies NPC's motion to preclude Dr. Ray from testifying causation regarding ONJ could have been reached in 2003 at the time Dr. Marx's reports became available.

## VI. February 29, 2012 Hearing

At the February 29, 2012 hearing, all parties agreed not to use or reference the term "meta-analysis" or to raise it in any way, shape, or form during the trial.

IT IS SO ORDERED.

Dated this 8th day of March, 2012, at Jefferson City, Missouri.

/s/ Matt J. Whitworth

MATT J. WHITWORTH
United States Magistrate Judge